Investigation of the temporal plasma cytokine/chemokine profile of the monosodium iodoacetate rat model of osteoarthritis: relevance to pharmacological reversal of hyperalgesia



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Introduction

- Osteoarthritis (OA) is estimated to affect 10-15% of individuals over the age of 60 (World Health Organisation, 2013)
- OA affects load bearing joints and often leads to pain and disability
- Identifying biomarkers associated with efficacy of pharmacological interventions will facilitate drug discovery in OA

Aims:

- 1) Investigate the pharmacological efficacy of gold standard analgesic drugs in the monosodium-iodoacetate (MIA) rat model of OA
- 2) Examine the temporal plasma cytokine/chemokine profile in the MIA model of OA

Methods

The OA model was induced in 3 cohorts of male Sprague-Dawley rats (n=105) by intra-articular injection (knee joint) of the glycolysis inhibitor MIA (80mg/ml; 0.025ml/rat)

Weight-bearing was measured using an incapacitance meter at baseline and hyperalgesia induced by MIA was measured

Cohort 1:

- Days 3-7 (early phase): Daily administration of vehicle, celecoxib (50mg/kg, PO) or pregabalin (30mg/kg, PO)

Cohort 2:

- Days 24-28 (late phase): Daily administration of vehicle, celecoxib (50mg/kg, PO) or pregabalin (30mg/kg, PO)

Cohort 3:

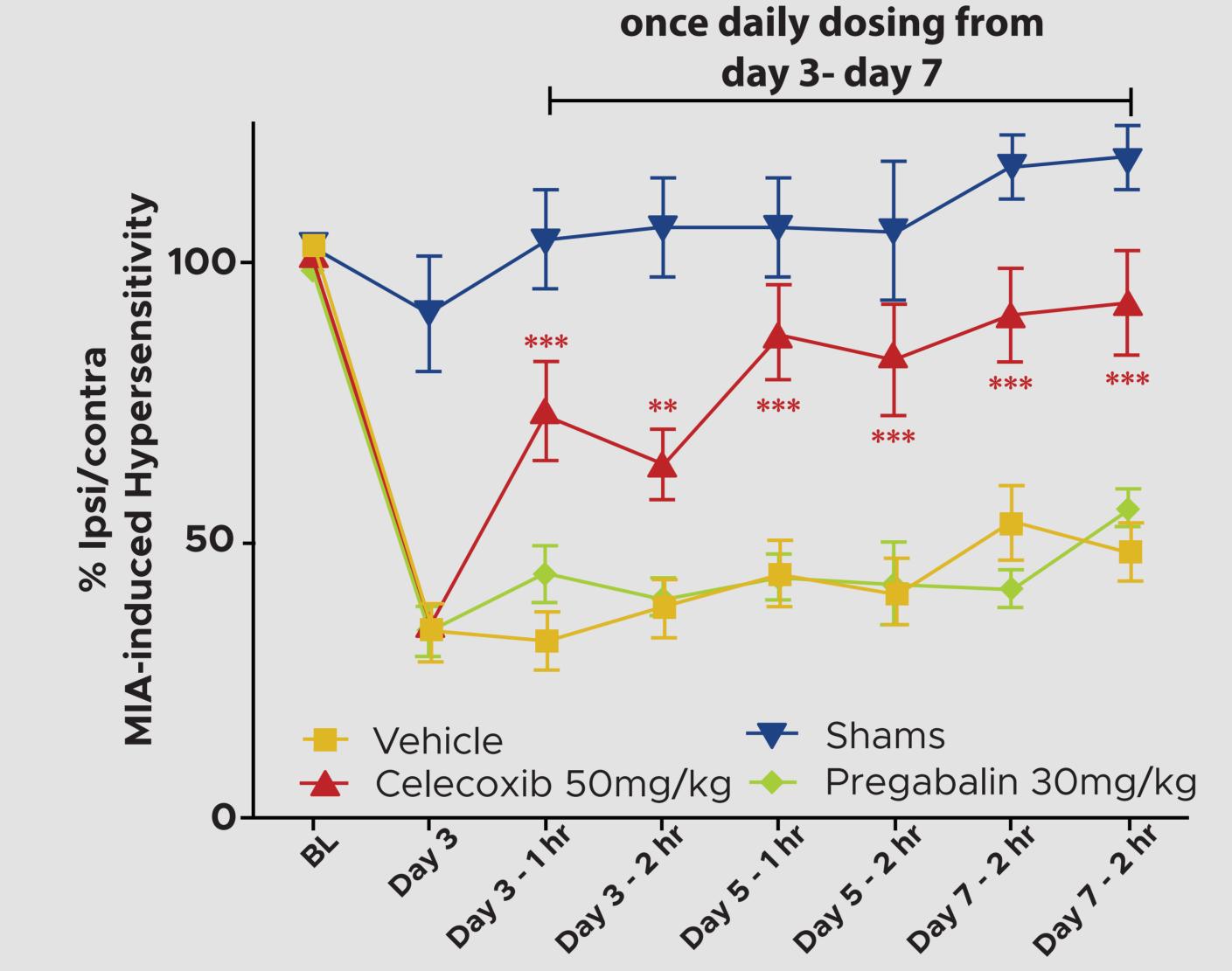
- Days 0, 4, 7, 14: Blood sampling and plasma isolation

Plasma cytokines/chemokines were analysed using an MSD multiplexed assay

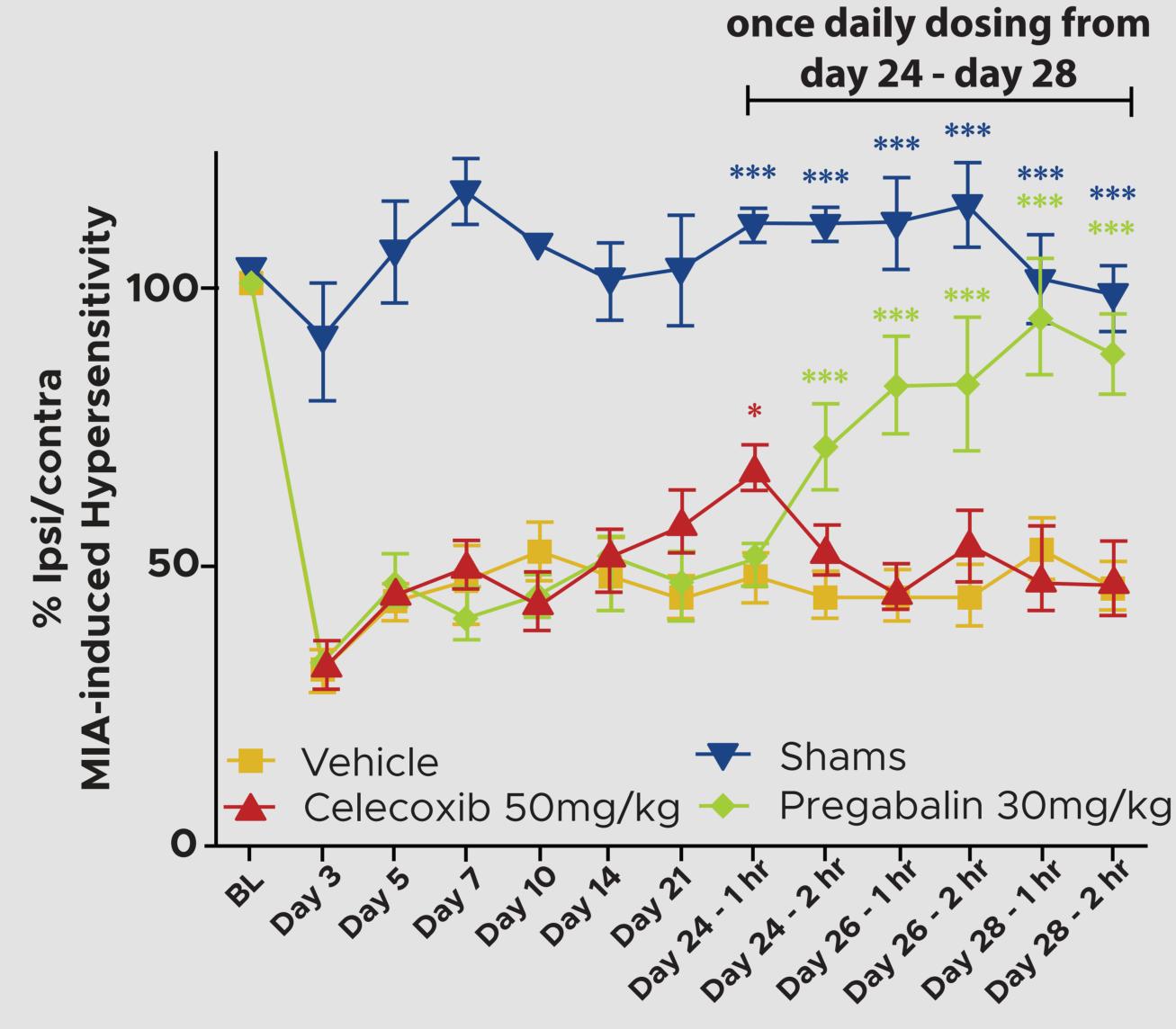


Results

Early phase (days 3-7): Effects of celecoxib and pregabalin on hyperalgesia



Late phase (days 24-28): Effects of celecoxib and pregabalin on hyperalgesia



*P<0.05, ***P<0.001, Values are mean ± SEM, Repeated measures ANOVA

Conclusions

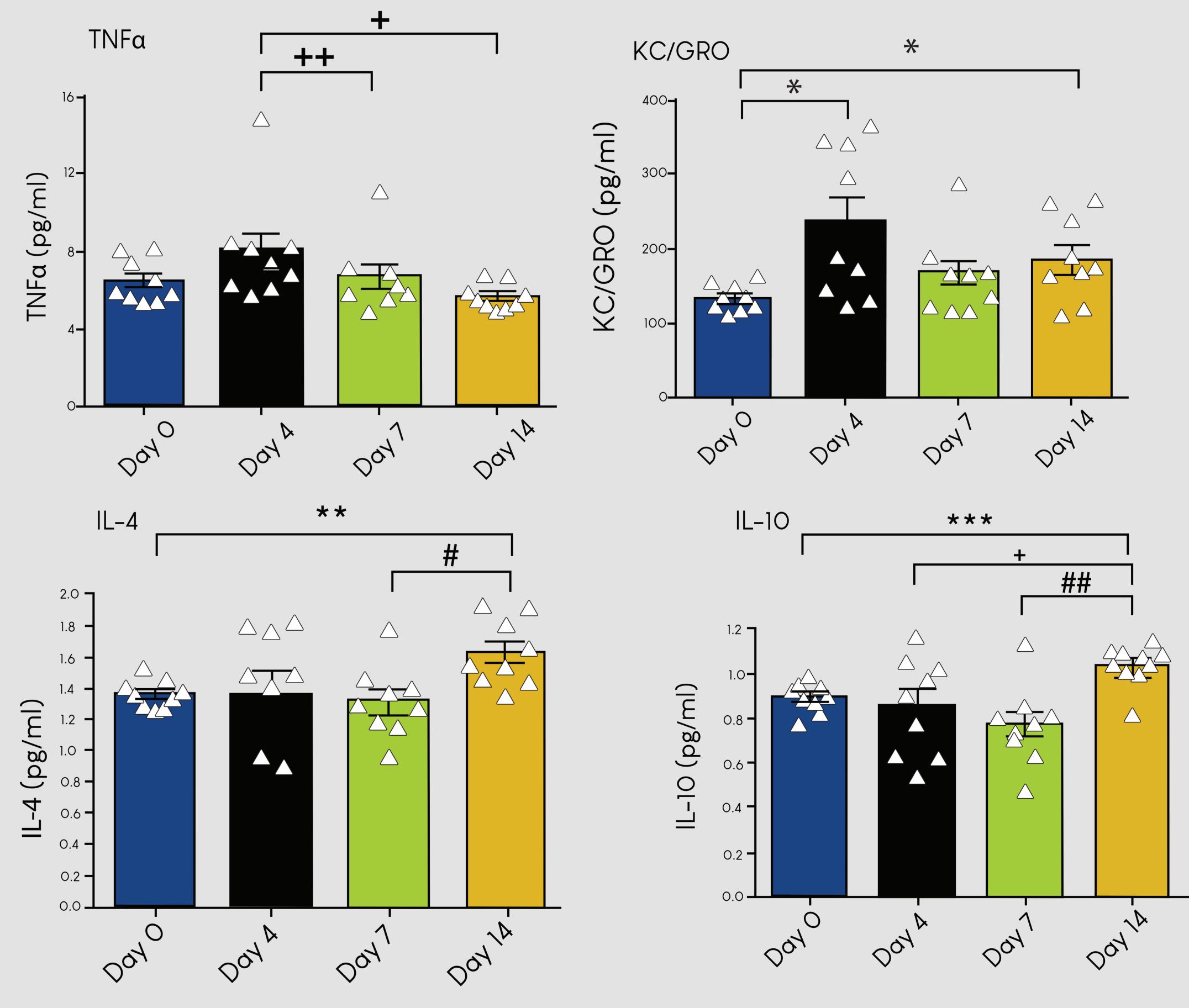
- Hyperalgesia was reversed by the non-steroidal anti-inflammatory drug (NSAID) celecoxib during the early inflammatory phase of the model
- Pregabalin reversed hyperalgesia during the late neuropathic phase
- The inflammatory mediator KC/GRO is acutely increased in plasma after OA induction
- The pro-inflammatory cytokine TNFa was decreased in plasma from day 3 after MIA administration
- The anti-inflammatory cytokines IL-4 and IL-10 are increased in plasma after the inflammatory phase of the model

- These data suggest plasma inflammatory markers may indicated OA disease progression and could be used to inform treatment strategy

Results

Plasma: Cytokine/Chemokine expression

pg/ml	Day O	Day 4	Day 7	Day 14
IFNγ	5.99 ± 0.21	5.36 ± 0.92	4.40 ± 0.61	6.03 ± 0.57
IL-13	4.63 ± 0.47	4.25 ± 0.43	3.44 ± 0.36	3.8 ± 0.26
IL-6	24.8 ± 4.2	32.7 ± 8.9	ND	23.4 ± 8.4
IL-5	ND	ND	ND	ND
IL-1β	ND	ND	ND	ND



*P<0.05, **P<0.01, ***P<0.001

+P<0.05, ++P<0.01

#P<0.05, ##P<0.01

Values are mean ± SEM, Repeated measures ANOVA

Contact



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